Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1-75. (Canceled)

76. (Previously Presented) A Factor VII or Factor VIIa polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising an amino acid substitution selected from a hydrophobic amino acid residue or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

77-79. (Canceled)

80. (Previously Presented) The polypeptide of claim 76, wherein a phenylalanine, leucine or isoleucine residue is substituted at position 34.

81. (Previously Presented) The polypeptide of claim 76, wherein a glutamic acid residue is substituted at position 34.

82-84. (Canceled)

85. (Previously Presented) The polypeptide of claim 76, further comprising an amino acid substitution at position 10.

86. (Previously Presented) The polypeptide of claim 85, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.

87. (Previously Presented) The polypeptide of claim 86, wherein a glutamine residue is substituted at position 10.

88. (Previously Presented) The polypeptide of claim 76, further comprising an amino acid substitution at position 32.

89. (Previously Presented) The polypeptide of claim 88, wherein a glutamic acid residue is substituted at position 32.

90. (Previously Presented) The polypeptide of claim 76, further comprising an amino acid substitution at position 28.

91. (Previously Presented) The polypeptide of claim 90, wherein a phenylalanine or a glutamic acid residue is substituted at position 28.

92. (Previously Presented) The polypeptide of claim 91, wherein a phenylalanine residue is substituted at position 28.

93. (Previously Presented) The polypeptide of claim 76, further comprising an insertion at position 4.

94. (Previously Presented) The polypeptide of claim 93, wherein a tyrosine or glycine residue is inserted at position 4.

95. (Previously Presented) The polypeptide of claim 94, wherein a tyrosine residue is inserted at position 4.

96. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an amount of a Factor VII or Factor VIIa polypeptide effective to increase clot formation, wherein said Factor VII or Factor VIIa polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising an amino acid substitution selected from a hydrophobic amino acid residue or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

97. (Previously Presented) The pharmaceutical composition of claim 96, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.

98. (Previously Presented) An isolated mammalian host cell that expresses a Factor VII or Factor VIIa polypeptide, said Factor VII or Factor VIIa polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising an amino acid substitution selected from a hydrophobic amino acid residue or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

99. (Previously Presented) A method of increasing clot formation in a mammal comprising administering an amount of a Factor VII or Factor VIIa polypeptide effective to increase clot formation in said mammal, wherein said Factor VII or Factor VIIa polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising an amino acid substitution selected from a hydrophobic amino acid residue or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

100. (Previously Presented) A method for treating a bleeding disorder in a patient, said method comprising administering the pharmaceutical composition of claim 96 to said patient.

101. (Previously Presented) An isolated nucleic acid molecule comprising a nucleic acid sequence encoding the polypeptide of claim 76.

102. (Previously Presented) A method for producing a Factor VII or Factor VIIa polypeptide having a modified GLA domain comprising an amino acid substitution selected from a hydrophobic amino acid residue or a glutamic acid residue at position 34, wherein amino

acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3, the method comprising (a) providing a culture of the mammalian host cell of claim 98 under conditions which permit expression of the polypeptide, and (b) recovering the polypeptide.

103-116. (Canceled)

117. (New) The polypeptide of claim 76, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.

118. (New) The pharmaceutical composition of claim 96, wherein a glutamic acid residue is substituted at position 34.

119. (New) The pharmaceutical composition of claim 96, further comprising an amino acid substitution at position 10.

120. (New) The pharmaceutical composition of claim 119, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.

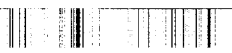
121. (New) The pharmaceutical composition of claim 120, wherein a glutamine residue is substituted at position 10.

122. (New) The pharmaceutical composition of claim 96, further comprising an amino acid substitution at position 32.

123. (New) The pharmaceutical composition of claim 122, wherein a glutamic acid residue is substituted at position 32.

124. (New) The host cell of claim 98, wherein a glutamic acid residue is substituted at position 34.

125. (New) The host cell of claim 98, further comprising an amino acid substitution at position 10.



126. (New) The host cell of claim 125, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.

127. (New) The host cell of claim 126, wherein a glutamine residue is substituted at position 10.

128. (New) The host cell of claim 98, further comprising an amino acid substitution at position 32.

129. (New) The host cell of claim 128, wherein a glutamic acid residue is substituted at position 32.

130. (New) The host cell of claim 98, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.

131. (New) The method of claim 99, wherein a glutamic acid residue is substituted at position 34.

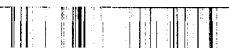
132. (New) The method of claim 99, further comprising an amino acid substitution at position 10.

133. (New) The method of claim 132, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.

134. (New) The method of claim 133, wherein a glutamine residue is substituted at position 10.

135. (New) The method of claim 99, further comprising an amino acid substitution at position 32.

136. (New) The method of claim 135, wherein a glutamic acid residue is substituted at position 32.



137. (New) The method of claim 99, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.

138. (New) The isolated nucleic acid of claim 101, wherein a glutamic acid residue is substituted at position 34.

139. (New) The isolated nucleic acid of claim 101, further comprising an amino acid substitution at position 10.

140. (New) The isolated nucleic acid of claim 139, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.

141. (New) The isolated nucleic acid of claim 140, wherein a glutamine residue is substituted at position 10.

142. (New) The isolated nucleic acid of claim 101, further comprising an amino acid substitution at position 32.

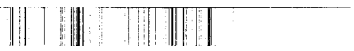
143. (New) The isolated nucleic acid of claim 142, wherein a glutamic acid residue is substituted at position 32.

144. (New) The isolated nucleic acid of claim 101, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.

145. (New) The method of claim 102, wherein a glutamic acid residue is substituted at position 34.

146. (New) The method of claim 102, further comprising an amino acid substitution at position 10.

147. (New) The method of claim 146, wherein a glutamine, asparagine, glutamic acid, or aspartic acid residue is substituted at position 10.



148. (New) The method of claim 147, wherein a glutamine residue is substituted at position 10.

149. (New) The method of claim 102, further comprising an amino acid substitution at position 32.

150. (New) The method of claim 149, wherein a glutamic acid residue is substituted at position 32.

151. (New) The method of claim 102, wherein the Factor VII or Factor VIIa polypeptide further comprises a glutamine residue substituted at position 10 and a glutamic acid residue substituted at position 32.